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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/134,771	08/12/1998	DINAH W.Y. SAH	860098.425	8421

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EXAMINER
KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
1636	26

DATE MAILED: 09/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N . 09/134,771	Applicant(s) SAH ET AL.	
	Examiner S. Kaushal	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,13-15 and 23-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,13-15 and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 06/19/02 has been acknowledged.

Claims 11-12 were canceled.
Claim 27 was newly filed.
Claims 1, 6, 9 and 25-26 were amended.
Claims 1-10, 13-15 and 23-27 were pending and were examined in this office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

► *If the claims are amended, added and/or canceled in response to this office action the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (http://www.uspto.gov) and A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED.*

Claim Rejections - 35 USC § 103

Claims 1-10, 13-15 and 23-27 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Hosimaru et al (PNAS. 93:1518-1523, 1996, *ref of record*) and Prasad et al (In Vitro. Cell Dev. 30A:596-603, 1994, *ref of record*) in view of Boss et al (US 5411883, 1995, *ref of record*), Weiss et al (US 5750376) and Gallyas et al (Neurochem. Res. 22(5):569-575, 1997, *ref of record*).

The applicant argues that there is no suggestion or motivation to combine the cited references and there is no reasonable expectation of success (response, page 4, sec. A). The

applicant argues that cited references do not teach the method as claimed and use of FGF-2, EGF and PDGF together. The applicant argues that Boss does not describe the production of monolayers of cells as recited in the instant invention. The applicant argues that neuronal progenitor cells described in Boss are substantially different from those described in the instant application (response, page 5, para.2). The applicant argues that rat cells as disclosed by Hosimaru and Parsad are substantially different from human cells as two comes from different sources (response, page 5, para.3). The applicant argues that the fact that one cell may substitute for another does not mean that second is obvious in light of the first (response, page 6, para.1). The applicant argues that general method of making immortalized rat neuronal progenitor cells as taught in Hoshimaru cannot render obvious the claimed conditionally-immortalized human mesencephalon cells it self (response, page 6, para.2). The applicant argues that a person skill in the art would not expect that the method of immortalizing rat neuronal progenitor as taught by Hosimaru and Parsad would also work for human mesencephalonic neuronal cell progenitors in view of Boss (response, page 6, sec. C). The applicant further argues that claims have been amended to recite a combination of growth factors claimed (response, page 7, para.2). The applicant argues that prior to present invention those ordinary skilled in the art would not have any success in using the teaching of Hosimaru or Parsad for human mesencephalic cells (response, page 7, para.3). The applicant argues that Boss and Gallyas does not remedy Hosimaru and Parsad deficiencies as neither disclose the applicants conditions suitable for producing conditionally immortalized human mesencephalic neural progenitor cells (response, page 8, para.2). In addition, the applicant argues that Gallyas teaches nothing relevant to invention as claimed (response, page 8, para.3).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

The applicant fails to consider the combined teaching of the reference cited herein in entirety. The combination and modification of the teachings of the prior art clearly suggested the claimed invention. The arguments taken as a whole rely heavily on the deficiencies of each reference taken alone. One cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In this case, Hosimaru teaches immortalized rat neuronal progenitor cells wherein the expression of v-myc oncogene is driven by a tetracycline-controlled trnsactivator and a human cytomegalovirus (CMV) promoter. The cited art teaches that cells were first cultured in a serum supplemented media follow by culturing in serum free media containing growth factors. Hosimaru et al teaches the culturing and selection of the cells onto polyornithine/laminin-coated tissue culture plates. In addition, Hosimaru et al further teaches that presence of several cytokine, forskolin or growth factors is required for the differentiation of immortalized neuronal precursor cells (page 1518, abstract; page 1519, col.1. para.3; page 1522, col.1, para.2). Prasad et al teaches the isolation of an immortalized dopamine-producing nerve cell line derived from fetal rat mesencephalic tissue transfected with an oncogene. Prasad clearly teaches that mesencephalic cell could be genetically manipulated (see abstract).

Boss teaches the isolation and culture methods for the proliferation of human mesencephalon neuron progenitor cells, wherein the cultured neuronal cells differentiate to produce dopamine-producing cells (see abstract; col.6, line 33; col.9-10, table 1-3; col.20 line 60). In addition, Boss et al clearly teaches the isolation and monolayer culture of human mesencephalon neuron progenitor cells in details (see abstract; preparation of monolayer culture, col.11 line 25).

Weiss teaches a method for producing genetically modified multipotent neuronal stem cells and their progeny. The cited art teaches the use a combination of proliferation inducing growth factors selected from NGF, BDNF, NT-3, NT-4, NT-5, CNTF, FGF-1, FGF-2, EGF TGFa, TGFb, PDGF, IGFs and interleukins (col. 17, line 1-15; col.22, line 17-29). The cited art further teaches in-vitro proliferation of neuronal progenitor cells in the presence of above mentioned growth factors (col. 30 line 17; col.31, lines 46-64, examples 1-8).

Gallyas et al teaches the characterization of mouse immortalized neuronal cell lines by measuring the concentration of various neurotransmitters, like GABAergic and dopamine (see abstract; page 570, col.2, para 3; page 571, table-I, fig-1; page 572, table-II). Gallyas clearly provides method to characterize neuronal cells by the identification of GABAergic and dopamine expression as required by claim 7 and 8 of instant invention.

Thus, it would have been obvious to one ordinary skill in the art at the time the invention was made to substitute the immortalized rat neuronal progenitor cells as taught by Hosimaru et al and Prasad et al with human mesencephalon neuron progenitors cells as taught by Boss et al. It would have been further obvious to characterize immortalized human mesencephalon cells as taught by Gallyas et al because dopamine and GABA are neurotransmitter of interest. It would have been further obvious to use a combination of BDNF, CNTF, FGF-2, EGF, PDGF, and IGFs to promote the survival of mesencephalonic dopaminergic neurons in culture as taught by Weiss. One would have been motivated to make immortalized human neuronal progenitor cells wherein the expression of v-myc oncogene is driven by tetracycline-controlled trnsactivator because the suppression of v-myc oncogene in an immortalized progenitor induces the differentiation of the neuronal progenitor cell. Furthermore, immortalized human neuronal progenitor cells are valuable research tools to understand the molecular mechanism that control the development and function of nervous system cells in-vitro. In addition, one would have a reasonable expectation of success because neuronal progenitor cells are easy to transfect, especially in the presence of proliferation enhancing growth factors, which promotes cell survival. Furthermore, in view of cited art phenotypic characterization of GABAergic and dopaminergic neuronal cells has been considered routine in the art at the time of filing. Thus, the invention as claimed is prima facie obvious in view of prior art of record.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Irem Yucel Ph.D. can be reached on (703) 305-1998. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Zeta Adams, whose telephone number is (703) 305-3291.

S. Kaushal
Patent examiner

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER